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Impaired recognition of facial expressions of anger in Parkinson's disease patients acutely withdrawn from dopamine replacement therapy

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Abstract

We have previously reported that acute dopaminergic blockade in healthy volunteers results in a transient disruption of the recognition of facial expressions of anger, whilst leaving intact the recognition of other facial expressions (including fear and disgust) and facial identity processing. Parkinson's disease (PD) is characterised by cell loss in dopaminergic neuronal populations, and hence we predicted that PD would be associated with impaired anger recognition. We reasoned that treatment with dopamine replacement therapy (DRT) could mask any deficit present in PD, and therefore studied facial expression recognition in a group of PD patients transiently withdrawn from DRT. Seventeen PD patients were compared to 21 age- and IQ-matched controls on the Ekman 60 task, which required the forced-choice labelling of 10 exemplars of each of six facial expressions (anger, disgust, fear, sadness, happiness, surprise). In line with our predictions, PD patients showed a selective impairment in the recognition of facial expressions of anger. This deficit was not related to the PD patients' performance on the Benton unfamiliar-face matching task, which was normal, nor was the deficit related to overall disease severity, or to depression symptoms. However, as predicted by simulation theories, impaired anger recognition in PD was related to reduced levels of the anger-linked temperament trait, exploratory excitability. The results extend our previous findings of a role for dopamine in the processing of facial expressions of anger, and demonstrate the power of adopting a phylogenetic, comparative perspective on emotions.

Keywords: Anger; Dopamine; Emotion; Novelty seeking; Reward; Simulation theory

1. Introduction

Neuropsychology has provided evidence of strikingly selective impairments in the recognition of facial expressions of fear (Adolphs, Tranel, Damasio, & Damasio, 1994; Calder et al., 1996; Sprengelmeyer et al., 1999) and disgust (Adolphs, Tranel, & Damasio, 2003; Calder, Keane, Manes, Antoun, & Young, 2000). Clear double dissociations have been found between impaired recognition of facial expressions of these emotions (Calder, Lawrence, & Young, 2001), suggesting that different neural systems are specialised, at least in part, for the recognition of different classes of emotion expression, presumably related to their evolutionary history (Lawrence & Calder, 2004). A notable feature of such impairments in the recognition of conspecific facial expressions is that they reliably co-occur with alterations in the experience of the same emotion. These findings have been taken as support for 'simulationist' models of facial emotion recognition, in which the emotion states of others are recognised by mental simulation, i.e. by generating similar states in oneself (Goldman & Sripada, 2005; Gordon, 1992).

An outstanding question is whether evidence of selective impairments in the recognition of facial expressions of emotions other than fear and disgust can be found. Following Griffiths (2001), we have argued (Lawrence & Calder, 2004) that research on emotion expression recognition could benefit from the adoption of a phylogenetic perspective—that is, a search for emotion processing systems in humans that are elaborations of mechanisms seen in other species.

Two main motivational systems govern mammalian conspecific aggression. One controls offensive aggression and the other defensive aggression (Blanchard & Blanchard, 1984, 1988, 1989, 2003). Offensive aggression occurs in the context of conspecific challenge over adaptively important resources. It involves a set of species-typical behaviours enabling the individual to pursue and contact particular body sites on the opponent where blows (in humans including slaps and over-arm

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or closed-fist blows) are delivered. Its successful outcome is the termination of the resource dispute. There is evidence for behavioural homology in the expressions/signals (the two terms need not be strongly differentiated—Ekman, 1997) of offensive attack across several mammalian species, including, in primates, characteristic facial expressions (Blanchard & Blanchard, 1984, 1988, 1989; Chevalier-Skolnikoff, 1973; Darwin, 1872/1965; Ekman, 1972). The emotional basis of offensive aggression is thought to be homologous (in mammals) with (certain instances of) human anger (Blanchard & Blanchard, 1984).

In contrast, defensive attack occurs in the context of immediate threat to the individual, from either a conspecific or non-conspecific, e.g. a predator. Defensive attack is seen only when the individual is defending its own body, not when it is attacking another animal to "defend" a disputed resource. The latter situation involves offensive attack. Defensive attack includes a salient threat component (not seen in offensive attack), and involves a set of species-typical behaviours different from those seen in offensive attack, e.g. loud vocalizations and display of "weapons" (e.g. claws). The bites or blows delivered tend to be made on different body sites on the opponent than those contacted in offensive aggression. The successful outcome of defensive aggression is discouragement of the body-threatening conspecific or predator. There is evidence for behavioural homology in the expressions of defensive attack across several mammalian species, including, in primates, characteristic facial expressions (Blanchard & Blanchard, 1984, 1988, 1989; Blanchard, Hynd, Minke, Minemoto, & Blanchard, 2001; Chevalier-Skolnikoff, 1973; Darwin, 1872/1965; Ekman, 1972). The emotional basis of defensive aggression is thought to be homologous (in mammals) with (certain instances of) human fear (Blanchard et al., 2001).

Comparative neuropsychological research has suggested that specific mammalian neural systems are involved in offensive aggression. For example, post-mortem radioenzymatic and in vivo microdialysis experiments in rats have shown that hypothalamic and ventral striatal dopamine levels are elevated in anticipation of, and during, conspecific aggressive encounters (Barr, Sharpless, & Gibbons, 1979; Ferrari, van Erp, Tornatzky, & Miczek, 2003; Louilot, LeMoal, & Simon, 1986; van Erp & Miczek, 2000). Further, acute administration of dopamine antagonists, including those of the D2 receptor, such as sulpiride, or dopamine release inhibitors, selectively impairs offensive aggression in rodents (Aguilar, Miñarro, Pérez-Iranzo, & Simòn, 1994; Felip, Rodríguez-Arias, Aguilar, & Miñarro, 2001; Kudryavtseva, Lipina, & Koryakina, 1999; Masur, Maroni, & Benedito, 1975; Redolat, Brain, & Simón, 1991; Simón, Minarro, Redolat, & Garmendia, 1989), whilst leaving intact general locomotion. In primates, the dopamine-rich rhinal cortex (Lewis & Sesack, 1997) is another region implicated in offensive aggression (Meunier & Bachevalier, 2002). The system(s) involved in offensive aggression appear dissociable from an amygdala-centred system underpinning fear states, including those motivating defensive aggression against both conspecifics and predators (Blanchard & Takahashi, 1988; Meunier & Bachevalier, 2002; Oakes & Coover, 1997).

Given the role of dopamine in mammalian offensive aggression, together with evidence for behavioural homology in mammalian expressions of offensive aggression, and the predictions of simulation theory – that impairments in the ability to generate an emotion state would impair recognition of that same emotion expressed in the faces of conspecifics – we predicted that dopaminergic manipulations that reduce offensive aggression in other mammals would impair recognition of conspecific offensive aggression expressions, specifically, facial expressions of anger, in humans. In line with these predictions, we have shown that acute dopaminergic blockade in healthy volunteers results in a transient disruption of the recognition of facial expressions of anger (Lawrence, Calder, McGowan, & Grasby, 2002). In a within-subject, double-blind, placebo-controlled cross-over experiment, we found that acute dopaminergic blockade, produced by the administration of sulpiride (a dopamine D2 receptor antagonist) produced a selective disruption in the recognition of anger facial expressions, but left intact the recognition of other facial expressions (including fear and disgust), and facial identity processing (as measured by the Benton unfamiliar-face matching task).

Parkinson's disease (PD) is characterised by cell loss in dopaminergic neuronal populations (Hornykiewicz & Kish, 1986) and hence the prediction is that PD would be associated with impaired anger recognition. We reasoned that treatment with dopamine replacement therapy (DRT) could mask any deficit present in PD, and therefore studied facial expression recognition in a group of PD patients transiently withdrawn from DRT. We tested the hypothesis that, when acutely withdrawn from DRT, PD patients, relative to age- and IQ-matched healthy volunteers, would show impaired recognition of facial expressions of anger, whilst showing relatively spared recognition of other emotions and facial identity processing. Further, based on previous findings of paired deficits in emotion recognition and emotion experience, consistent with simulationist models of emotion recognition, we predicted that impaired anger recognition in PD would be linked to impaired anger experience. Exploratory excitability, a sub-component of novelty seeking (NS), as measured by Cloninger's tridimensional personality questionnaire (TPQ, Cloninger, 1987b) is an anger-linked temperament trait (Cloninger, 1987a), levels of which are reduced in PD (Fuji, Harada, Ohkoshi, Hayashi, & Yoshizawa, 2000). It predicts trait levels of outwardly directed anger in large samples of healthy volunteers (Giancola, Zeichner, Newbolt, & Stennett, 1994; Svrakic, Przybeck, Whitehead, & Cloninger, 1999). Notably, a similar relationship between exploratory excitability and offensive aggression appears to exist in rats (Kazlauckas et al., 2005). We predicted that anger recognition in PD would be correlated with levels of the anger-linked trait exploratory excitability.

2. Methods

2.1. Participants

Seventeen PD patients (7 females) were compared to 21 age ($t(36) = 0.60$, $P = 0.56$) and reading-estimated IQ (Nelson, 1991) ($t(36) = 0.29$, $P = 0.78$)-

Table 1
Demographic and clinical characteristics

Group	*n*	F:M	Age	Nart-IQ	UPDRSIII	BDI
PD	17	7/10	56.5(8.3)	117.5(5.3)	22.7(6.0)	8.7(5.4)
Controls	21	10/11	58.0(7.0)	118.1(8.4)	N/A	N/A

NB data are mean (S.D.) values. F:M = female:male ratio; Nart-IQ, IQ estimated using National Adult Reading Test—Revised Version; UPDRSIII, Unified Parkinson's Disease Rating Scale Part III motor score; BDI, Beck Depression Inventory.

matched healthy controls (10 females). All PD patients fulfilled Queen Square Brain Bank criteria for prospective diagnosis of PD (Hughes, Daniel, Kilford, & Lees, 1992). The severity of clinical symptoms was assessed when 'off' medication according to the Unified Parkinson's Disease Rating Scale Part III motor score (UPDRS III) (Fahn, Elton, & members of the UPDRS Development Committee, 1987). In addition, PD patients completed the Beck Depression Inventory (BDI) (Beck, 1987), a validated measure of depression symptoms in PD (Leentjens, Verhey, Luijckx, & Troost, 2000). Two of the PD participants had scores greater than the 16/17-point cut-off score recommended for diagnosing the presence of depression in PD. All patients included in the study were receiving daily dopamine replacement therapy (Levodopa preparations, and/or dopamine receptor agonists (ropinirole, cabergoline)). All were stable on their medication doses and responding well. Patients were asked to abstain from taking their medication the night before the assessment was scheduled to take place. Levodopa is eliminated from plasma with a half-life of 1–2 h (Gancher, Nutt, & Woodward, 1987). Demographic and clinical details are summarised in Table 1. Imperial College Research Ethics Committee approved the study, and all participants gave written informed consent.

3. Materials

3.1. Unfamiliar-face matching (Benton, Hamsher, Varney, & Spreen, 1983)

On each trial of the Benton unfamiliar-face matching task, the participant is shown a target face and an array of six faces; the task is to find further examples of the target face from amongst the array of six. Changes in head orientation and lighting can occur between the target and array faces.

3.2. Forced-choice labelling of facial expressions ('Ekman 60'; Calder et al., 1996)

Photographs of 10 models (6 females) were selected from the Ekman and Friesen (1976) Pictures of Facial Affect series. Each model displayed six facial expressions corresponding to six emotions: anger, disgust, fear, sadness, happiness and surprise: a total of 60 pictures. The 10 models were selected so that each emotion was well recognised by Ekman & Friesen's normative sample.

A forced-choice labelling procedure, widely used in research on facial expression recognition (Frank & Stennett, 2001) was adopted. Pictures were presented individually in random order and participants were asked to select one of six emotion labels (anger, disgust, fear, sadness, happiness, surprise) that best described the facial expression shown; no feedback was given as to the appropriateness of any response. The labels were visible throughout testing and participants were allowed as much time as they needed to make their selection.

3.3. Tridimensional personality questionnaire (Cloninger, 1987a, 1987b)

The version of the TPQ used in the present study was a 100-item, self-administered, true-false instrument. The TPQ was designed to assess 12 primary sub-scales, 4 for each of the three higher order temperament dimensions defined by Cloninger's theory: novelty seeking, harm avoidance (HA), and reward dependence (RD) (consistent with Cloninger's revised model, we scored persistence (RD2) as a separate primary dimension from the other 'social' reward dependence sub-scales). The TPQ scales have good internal consistency ($\alpha = 0.82$ for NS in an English sample, although NS1 (exploratory excitability) appears somewhat distinct, factor-analytically, from the other NS scales (Otter, Huber, & Bonner, 1995)). We scored each of the sub-scales as the sum over the items making up the sub-scales.

Our primary focus was on the relationship between the anger-linked NS sub-scale exploratory excitability (NS1) and anger recognition scores in PD patients. Examples of NS1 items include: "*When nothing new is happening, I usually start looking for something that is thrilling or exciting*", and "*In conversations I am much better as a listener than as a talker*" (reverse scored). We also examined, in an exploratory fashion, the relationship between emotion recognition performance and scores on the other TPQ sub-scales.

4. Results

4.1. Unfamiliar-face matching

PD patients scored within the normal range (41–54) (Benton et al., 1983) for this test (mean 48.4, S.D. 4).

4.2. Ekman 60

Results for the Ekman 60 test are presented in Fig. 1. The data were submitted to a repeated measures analysis of variance (ANOVA) with Huyn-Feldt correction for non-sphericity. Expression (anger, disgust, fear, sadness, happiness, surprise) was the within-subject factor and group (control, PD) the between-subject factor. The results of the ANOVA revealed no main effect of group, $F(1, 36) = 0.1$, $P = 0.76$, but a main effect of emotion, $F(3.8, 137.3) = 20.9$, $P < 0.001$, which was qualified by a significant interaction between emotion and group, $F(3.8, 137.3) = 2.5$, $P < 0.05$. A planned *t*-test comparison revealed that the PD patients showed impaired recognition of anger, $t(36) = -1.7$, $P < 0.05$ (one-tailed), but not of any other expression (all $P > 0.2$, two-tailed, except fear, $P > 0.1$ (two-tailed), with PD patients showing better performance than controls). The effect size for the anger contrast was calculated using the

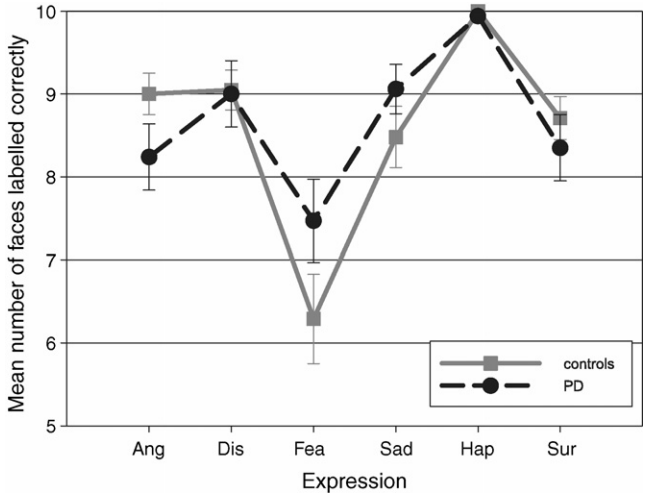

Fig. 1. Group mean numbers of expressions labelled correctly as a function of emotion portrayed (Ang, anger; Dis, disgust; Fea, fear; Sad, sadness; Hap, happiness; Sur, surprise) in Parkinson's disease patients acutely withdrawn from dopamine replacement therapy (PD) and healthy volunteers (controls). Error bars indicate ± S.E.M.

Table 2
Correlation matrix (PD participants only)

Expression	Benton	UPDRS III	BDI
Anger	0.20	0.37	−0.25
Disgust	0.40	−0.06	0.45
Fear	0.08	−0.24	0.08
Sad	0.42	−0.54*	0.36
Happy	0.41	−0.03	−0.08
Surprise	−0.25	−0.29	0.41

NB data are Spearman rank order correlation coefficients. Benton, Benton unfamiliar-face matching test; other abbreviations as for Table 1.
* $P < 0.05$.

formula for unequal sample sizes in two groups described by Rosenthal, Rosnow, & Rubin (2000, p. 31). This revealed an effect size $d = -0.56$ [null-counternull interval (0.00, −1.12)], a medium effect size according to Cohen's (1988) conventions. To further examine the effect of PD on the recognition of non-anger expressions, we combined recognition scores across all non-anger expressions to form a single non-anger expression category. The two groups did not significantly differ on non-anger expression recognition, $t(36) = 0.31$, $P = 0.76$.

Spearman rank correlation coefficients were computed to examine the relationship between facial expression recognition scores in the PD group and (a) scores on the Benton unfamiliar-face matching task; (b) UPDRS III motor scale scores; and (c) Beck Depression Inventory scores (see Table 2). Neither anger nor non-anger recognition scores were significantly correlated with performance on the Benton unfamiliar-face matching test; nor with BDI scores. Anger recognition was not significantly correlated with UPDRS III motor scores, although scores for sadness recognition were.

4.3. Are deficits in anger recognition and anger experience in PD linked?

To examine the hypothesised relationship between reduced anger recognition scores and reduced anger-linked temperament traits in PD, we calculated a Spearman partial correlation (Shipley, 2000, p. 88) between anger recognition scores and exploratory excitability (NS1) scores from the TPQ in the PD group, controlling for the effects of disease severity (UPDRS part III motor scores) and current mood (BDI scores). As predicted there was a highly significant correlation ($\rho = 0.73$ (d.f. = 10), $P = 0.007$, see Fig. 2) between anger recognition and exploratory excitability, but anger recognition scores were not correlated with any other temperament sub-scale score. In particular, there was no significant relation between anger recognition and NS2 (impulsiveness) ($\rho = -0.21$) or between anger recognition and the fear/anxiety-linked trait harm avoidance ($\rho = -0.09$). An exploratory analysis (again using Spearman partial correlation, controlling for the effects of disease severity and current mood) revealed a significant correlation between sadness recognition in PD and both the RD3 (attachment) ($\rho = 0.62$, (d.f. = 10), $P = 0.03$) and RD4 (dependence) ($\rho = 0.67$ (d.f. = 10), $P = 0.018$) social reward dependence sub-scales, and a trend for a negative correlation between surprise recognition and the HA2 (fear of uncertainty) harm avoidance sub-scale ($\rho = -0.56$ (d.f. = 10), $P = 0.057$) (i.e. individuals high in fear of uncertainty tended to label surprise facial expressions as fear).

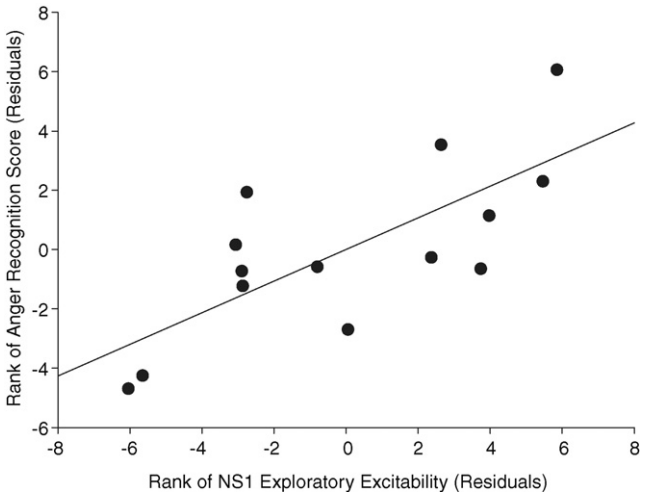

Fig. 2. Spearman partial correlation (controlling for UPDRS III and BDI scores) between anger recognition and exploratory excitability in PD patients.

5. Discussion

As predicted, Parkinson's disease patients, acutely withdrawn from dopamine replacement therapy, showed impaired recognition of anger facial expressions, but spared recognition of other emotion expressions and spared facial identity processing. Impaired anger recognition in PD was related to reduced levels of the anger-linked temperament trait, exploratory excitability. These findings have several implications.

Firstly, they provide additional evidence for selective disruption to the recognition of facial expressions of anger, supporting our previous findings of selectively impaired anger recognition following acute dopaminergic blockade in healthy volunteers (Lawrence et al., 2002). These results extend previous findings of selective or differential deficits in the recognition of fear (Adolphs et al., 1994; Calder et al., 1996; Sprengelmeyer et al., 1999) and disgust (Adolphs et al., 2003; Calder, Keane, Manes, et al., 2000) facial expressions.

There have been previous investigations of facial emotion expression recognition in PD. Several of these (Blonder, Gur, & Gur, 1989; Scott, Caird, & William, 1984; St. Clair, Borod, Sliwinski, Cote, & Stern, 1998) did not examine recognition of individual emotions, and so are difficult to interpret. A number of other investigations have, however, looked at the recognition of individual emotions. Some of these have found spared recognition of facial emotion expressions, using both forced-choice labelling and ratings tasks, in medicated PD patients with mild disease severity (Adolphs, Schul, & Tranel, 1998; Dewick, Hanley, Davies, Playfer, & Turnbull, 1991; Pell & Leonard, 2005). However, since patients in those studies were receiving DRT at time of testing, any dopamine-deficit linked impairment in anger recognition could have been masked. By contrast, other studies have reported deficits in the recognition

of several emotions in medicated PD patients. Such general impairments in emotion recognition in PD have been associated with clinical depression, with general perceptual or face processing impairments, with deficits in fluid intelligence, or with general cognitive decline related to increased disease severity (Breitenstein, Daum, & Ackermann, 1998; Dujardin, Blairy, Defebvre, Duhem et al., 2004; Kan, Kawamura, Hasegawa, Mochizuki, & Nakamura, 2002; Madeley, Ellis, & Mindham, 1995; Yip, Lee, Ho, Tsang, & Li, 2003).

In the study most comparable to ours, Sprengelmeyer et al. (2003) found that, relative to a control group of medicated PD patients, a group of never-medicated PD patients were impaired in the recognition of facial expressions of anger, and also disgust. Also, Dujardin, Blairy, Defebvre, Krystkowiak, et al. (2004) have reported that subthalamic nucleus stimulation, with a concomitant reduction in DRT, impairs facial emotion expression recognition in PD patients, particularly for expressions of anger, consistent with our findings.

A notable discrepancy between our study and that of Sprengelmeyer et al. (2003) is that our group of non-medicated PD patients was not impaired in recognising disgust faces. This is noteworthy, as on the basis of previous findings in patients with Huntington's disease (HD), who show a disproportionate (albeit non-selective) deficit in disgust recognition, it has been argued that the basal ganglia, including the striatum, are important for disgust recognition (Sprengelmeyer et al., 1996). Further, a single case (NK) who shows a profound and selective impairment in disgust recognition, has left-lateralised damage to both the insula and basal ganglia (Calder, Keane, Manes, et al., 2000). It is doubtful, however, that disgust recognition is reliant upon the striatum, or more specifically, its dopaminergic neuromodulation, which is compromised in PD (Hornykiewicz & Kish, 1986). Firstly, a patient with bilateral insula lesions, but intact basal ganglia, shows impaired disgust recognition (Adolphs et al., 2003), suggesting that insula damage alone is sufficient to impair disgust recognition. Secondly, HD patients, in addition to basal ganglia pathology, also show insula damage, even prior to the onset of manifest movement disorder (Thieben et al., 2002) and in an fMRI study of pre-symptomatic HD gene carriers, insula activity was significantly reduced whilst viewing disgust faces, relative to controls (Henenlotter et al., 2004). Also, we (Lawrence et al., 2002) showed that acute dopamine D2 receptor blockade in healthy males lead to a selective reduction in anger, not disgust, recognition. Finally, Calder, Keane, Lawrence, and Manes (2004) found that focal, non-progressive damage to the ventral putamen impairs anger recognition, whilst leaving intact disgust recognition. These data suggest that the striatum is not necessary for intact disgust recognition, which instead relies, in part, on ventral anterior regions of insula cortex (Krolak-Salmon et al., 2003). Given that insula pathology can occur in some PD patients (Kikuchi et al., 2001), it is possible that any disgust deficits in PD could result from such pathology, as opposed to striatal dopamine loss. It is also relevant that PD patients show intact reactions to disgusting tastes and odours (Saku & Ellgring, 1992; Sienkiewicz-Jarosz et al., 2005; Travers et al., 1993), unlike HD patients (Mitchell, Heims, Neville, & Rickards, 2005).

Calder et al.'s (2004) findings that ventral putamen lesions impair anger recognition, and an fMRI study showing ventral putamen activity during viewing of angry faces (Phillips et al., 1999), together with in vivo microdialysis data in rats showing dopamine release in the ventral, but not dorsal, striatum in anticipation of aggressive encounters (Ferrari et al., 2003), suggests that it is primarily dopamine projections to the ventral, rather than dorsal, striatum (and perhaps to other offensive aggression linked regions, such as hypothalamus and rhinal cortex) that are important for anger recognition. While the greatest cell loss in PD is in the ventrolateral tier of the substantia nigra pars compacta, from which the dorsolateral putamen – the region most affected in PD – receives dopaminergic input, a variable, less pronounced loss of neurons also occurs in the dorsal tier of the nigra (projecting to the caudate), in the retrorubral region (projecting to the hypothalamus), and in the ventral tegmental area (projecting to the ventral striatum, amygdala, hippocampus, and motor, premotor, rhinal, cingulate, and prefrontal cortices) (Hornykiewicz & Kish, 1986; Lewis & Sesack, 1997; Price, Farley, & Hornykiewicz, 1978; Scatton, Javoy-Agid, Rouquier, Dubois, & Agid, 1983). Intriguingly, there is an 'open-loop' projection between primary motor cortex (M1) – which is hypo-active in drug-naïve parkinsonian patients (Buhmann et al., 2003) – and the ventral putamen (Kelly & Strick, 2004). Also, thalamic regions connected to ventral striatum are severely affected by inclusion-body pathology in PD (Rüb et al., 2002). Further, when acutely withdrawn from DRT (as here) PD patients show reduced regional cerebral blood flow in brain regions receiving dopaminergic input from the ventral tegmental area, including rhinal cortex, during reward-seeking behaviour (Goerendt, Lawrence, & Brooks, 2004) and Remy, Doder, Lees, Turjanski, and Brooks (2005) found reduced dopamine transporter binding in the ventral striatum in PD associated with apathy, one manifestation of which is reduced novelty seeking (Daffner et al., 2000).

In our study, impaired anger recognition in PD was related to reduced exploratory excitability, a sub-component of novelty seeking, which has been shown to predict the reactivity of the ventral striatal dopamine system in healthy volunteers (Leyton et al., 2002), consistent with a role for ventral striatal dopamine systems in anger recognition. However, regions other than the ventral striatum have been implicated in anger recognition, including the anterior cingulate (Blair, Morris, Frith, Perrett, & Dolan, 1999; Harmer, Thilo, Rothwell, & Goodwin, 2001; Williams et al., 2005) and lateral orbitofrontal cortex (Blair et al., 1999), and these regions show reductions in dopamine levels in PD (Hornykiewicz & Kish, 1986; Scatton et al., 1983).

Our suggestions for a central role of ventral striatal dopamine systems in anger recognition may seem inconsistent with imaging data showing amygdala activity in participants viewing angry faces (e.g. Morris, Öhman, & Dolan, 1998; Whalen et al., 2001). Fear, an emotion in which the amygdala is critically involved (Davis, 2000), exerts a strong inhibitory influence on offensive, but not defensive, aggression (Blanchard & Blanchard, 1989), suggesting one explanation for amygdala involvement in the processing of angry faces in some circumstances (e.g., in situations where there is perceived threat to

bodily harm, or in phobic individuals (Öhman, 1986; Stein, Goldin, Sareen, Zorrilla, & Brown, 2002). Whilst it is possible that, in different instances, reduced anger recognition may be due to either a reduction in underlying offensive aggression systems or an enhancement of defensiveness, or an interaction of the two, the fear-linked trait, harm avoidance was not related to impaired anger recognition in PD in our study, suggesting the deficit is not solely attributable to, e.g., fear-induced avoidance of angry faces (Pine et al., 2005; but see Putnam, Hermans, & van Honk, 2004), but rather primarily to a reduction in underlying anger systems, mediated partly by ventral striatal-related dopamine systems.

Another possibility is that different sub-regions of, or different patterns of activity/neuromodulation within the amygdala are involved in anger versus fear. While there is little positive evidence of a role for the amygdala in offensive aggression in mammals (Blanchard & Takahashi, 1988; Meunier & Bachevalier, 2002; Oakes & Coover, 1997) or in anger in humans (Murphy, Nimmo-Smith, & Lawrence, 2003b) and amygdala lesions that impair defensive aggression leave intact offensive aggression in rats (Blanchard & Takahashi, 1988), such results can "Hardly be interpreted as indicating that there are no mechanisms relevant to offense represented [*sic*] in the area of the amygdala or surrounding cortex" (Blanchard & Takahashi, 1988, p. 616).

In our study, PD patients actually performed better than controls in fear recognition, which can be selectively impaired following amygdala lesions (Sprengelmeyer et al., 1999). Although not statistically significant, the effect size for this enhancement ($d = 0.52$) was comparable to that for the impairment in anger recognition. This is intriguing, as Frank, Seeberger, and O'Reilly (2004) found that PD patients acutely withdrawn from DRT display an enhanced ability to avoid punishing stimuli. Our findings could be taken as support for the suggestion (Blanchard & Blanchard, 1989) that fear- and anger-related motivational systems are mutually antagonistic. Studies in rats have found enhanced fear, together with increased amygdala activity, during acute withdrawal from high-dose schedules of dopaminergic drugs, such as cocaine and amphetamine (Murphy, Russig, Pezze, Ferger, & Feldon, 2003a; Mutschler & Miczek, 1998), findings potentially relevant to heightened fear sensitivity in PD patients withdrawn from DRT. As argued above, heightened fear sensitivity resulting from DRT withdrawal cannot, however, explain anger recognition deficits in PD, since never-medicated PD patients are also impaired in anger recognition (Sprengelmeyer et al., 2003).

The profile of impairment in our study—impaired anger recognition, but heightened fear recognition, together with previous findings of selective impairments in anger (Lawrence et al., 2002) and fear (Sprengelmeyer et al., 1999) recognition is problematic for the view that there is a single (amygdala-centred) neural system specialised for processing highly arousing, unpleasant emotions, of which fear and anger are two exemplars (Adolphs, Russell, & Tranel, 1999). Our data support theories in which certain systems are specialised, in part, but not exclusively, for the recognition of particular classes of emotion expression related to their evolutionary histories (Lawrence & Calder, 2004) and demonstrate the utility of adopting a comparative approach to emotions.

Our results are relevant to debates regarding mechanisms of emotion recognition. Simulation theories argue that the emotion states of others are understood by mental simulation, i.e. by generating similar states in oneself (Goldman & Sripada, 2005; Gordon, 1992). Such models predict that the same neural mechanisms subserve both emotion experience and emotion recognition. PD patients show reduced anger, even prior to the onset of overt movement disorder (Todes & Lees, 1985), and conversely, intake of large quantities of DRT (e.g. Levodopa) is associated with heightened anger in PD (Lawrence, Evans, & Lees, 2003) and depression (Goodwin, Murphy, Brodie, & Bunney, 1970). Here, we found that impaired anger recognition in PD was linked with reduced levels of the anger-linked trait, exploratory excitability. Exploratory excitability predicts self-report trait anger (Giancola et al., 1994; Svrakic et al., 1999; see also Wills, Vaccaro, & McNamara, 1994); is related to fun-seeking and reward-drive from the BAS scales (Carver & White, 1994), which predict self- and observer-report trait anger (Blair, Peters, & Granger, 2004; Heweg, Hagemann, Seifert, Naumann, & Bartussek, 2004; Smits & Kuppens, 2005; von Collani & Werner, 2005), anger in response to imagined scenarios (Carver, 2004; Smits & Kuppens, 2005) and anger during a cooperative computer game (Wingrove & Bond, 1998); and to sensation-seeking, which predicts desire to engage in aggression (Joireman, Anderson, & Strathman, 2003), and self-report trait anger (Dahlen, Martin, Ragan, & Kuhlman, 2004) (see also Wilson, Barrett, & Gray, 1989; Zuckerman, 1999). Further, mental imagery of anger-provoking scenarios activates the ventral striatum (Schaefer et al., 2003), consistent with the idea that ventral striatal dopamine systems underlie not only anger recognition, but also the generation of anger states.

According to "reverse simulation" accounts of emotion recognition (Goldman & Sripada, 2005) an attributor viewing an emotion-expressive face starts by (covertly) mimicking the facial expression she observes (Dimberg, Thunberg, & Elmehed, 2000). Such mimicry has a causal effect in generating, in attenuated form, the corresponding emotion state (Ekman, Levenson, & Friesen, 1983). An experiencer then classifies her own emotion state, and, in line with general simulationist notions, classifies the observed face as being expressive of the same state produced in herself (Goldman & Sripada, 2005). Consistent with this account, Jacobs, Shuren, Bowers, and Heilman (1995) found that PD patients were impaired in the production of facial expressions, particularly anger, and that this production deficit correlated with impaired expression recognition. Inconsistent with this account, however, is the finding that individuals with congenital facial paralysis show intact face-based emotion recognition (Calder, Keane, Cole, Campbell, & Young, 2000). Rather than actual reverse simulation involving the facial musculature, the observer viewing the facial expression displayed by the target may jump directly to somatosensory representations of what it would feel like to have made the requisite facial expression, which in turn serves to bring about the corresponding emotion state as in standard reverse simulation (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000;

Goldman & Sripada, 2005). We favour the idea that, rather than exclusively involving actual (covert) or "as if" facial mimicry, emotion recognition via simulation involves a general motor anticipation of the target's behaviour (Gordon, 1987, p. 148). The finding that ventral striatal dopamine is released in anticipation of offensive attack (Ferrari et al., 2003) supports this notion. Our data are also consistent with projection-based simulation mechanisms (Gordon, 1992). Regardless of the particular mechanism, our data, showing a correlation between impaired anger recognition and reduced levels of an anger-linked temperament trait, provide evidence in support of simulation theories of emotion recognition.

Finally, we will attempt to integrate the role of the ventral striatal dopamine system in anger and anger recognition via simulation with its broader role in incentive motivation and reward pursuit (Berridge & Robinson, 1998; Ikemoto & Panksepp, 1999). Success (or anticipated success) in offensive aggressive encounters involving conspecific challenge has a strong motivational component (in part since success in such contests will increase access to, control of, or possession of, desirable resources (Martinez, Guillén-Salazar, Salvador, & Simón, 1995; Tsang & Stutz, 1984) (see also Harmon-Jones, Sigelman, Bohlig, & Harmon-Jones, 2003 and compare Averill's (1982, p. 176) conclusion that "On a very broad level ... it would seem that anger is often subsidiary to the more inclusive goal of achieving personal control over a situation"), although there is a parallel and sometimes even more powerful motivation of hurting the other individual (Blanchard & Blanchard, 1989). The actions of seeking access to specific targets and systematically attacking these suggest a strong motivational 'pursuit' aspect to offensive attack, and individuals of several species, including humans, will exert considerable effort in order to be able to aggress (Blanchard & Blanchard, 1989; Fish, DeBold, & Miczek, 2002). This motivation, which is directed toward attack on an opponent in resource disputes, has been suggested to be homologous to human anger (Blanchard & Blanchard, 1984, 1989). There is clear evidence that the ventral striatum is a key part of a network of brain structures mediating such aggressive motivation (Davis & Marler, 2004; Miczek, Fish, De Bold, & De Almeida, 2002), and, in our study, impaired anger recognition in PD was predicted by levels of exploratory excitability. This trait relates to anger/aggressive motivation, and to incentive motivation in general, e.g., predicting drug wanting, and the reactivity of ventral striatal dopamine systems to drug rewards (Leyton et al., 2002). Further, lesions that reduce offensive aggression in rhesus monkeys reduce incentive motivation and reward pursuit more generally (Meunier & Bachevalier, 2002). We suggest that there is no neural system dedicated exclusively to anger and anger recognition via simulation, but rather, such abilities depend upon the functions of a broader neural system supporting reward pursuit and incentive motivation.

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References

Adams, D. B. (1981). Motivational systems of social behavior in male rats and monkeys: Are they homologous? *Aggressive Behavior*, *7*, 5–18.

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A.R. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature*, 372, 669–672.

Adolphs, R., Damasio, H., Tranel, D., Cooper, G., & Damasio, A. R. (2000). A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. *Journal of Neuroscience*, *20*, 2683–2690.

Adolphs, R., Russell, J. A., & Tranel, D. (1999). A role for the human amygdala in recognizing emotional arousal from unpleasant stimuli. *Psychological Science*, *10*, 167–171.

Adolphs, R., Schul, R., & Tranel, D. (1998). Intact recognition of facial emotion in Parkinson's disease. *Neuropsychology*, *12*, 253–258.

Adolphs, R., Tranel, D., & Damasio, A. R. (2003). Dissociable neural systems for recognising emotions. *Brain and Cognition*, *52*, 61–69.

Aguilar, M. A., Miñarro, J., Pérez-Iranzo, N., & Simòn, V. M. (1994). Behavioral profile of raclopride in agonistic encounters between male mice. *Pharmacology, Biochemistry and Behavior*, *47*, 753–756.

Averill, J. R. (1982). *Anger and aggression: An essay on emotion*. New York: Springer-Verlag.

Barr, G. A., Sharpless, N. S., & Gibbons, J. L. (1979). Differences in the level of dopamine in the hypothalamus of aggressive and non-aggressive rats. *Brain Research*, *166*, 211–216.

Beatty, W. W., Goodkin, D. E., Weir, W. S., Staton, R. D., Monson, N., & Beatty, P. A. (1989). Affective judgements by patients with Parkinson's disease or chronic progressive multiple sclerosis. *Bulletin of the Psychonomic Society*, *27*, 361–364.

Beck, A. T. (1987). *Beck Depression Inventory*. San Antonio, TX: Psychological Corporation.

Benton, A. L., Hamsher, K., Varney, N. R., & Spreen, O. (1983). *Contributions to neuropsychological assessment*. New York: Oxford University Press.

Berridge, K. C., & Robinson, T. E. (1998). What is the role of dopamine in reward: Hedonics, learning, or incentive salience? *Brain Research Reviews*, *28*, 308–367.

Blanchard, D. C., & Blanchard, R. J. (1984). Affect and aggression: An animal model applied to human behavior. In R. J. Blanchard, & D. C. Blanchard (Eds.), *Advances in the study of aggression*, (Vol. 1, pp. 1–62). New York: Academic Press.

Blanchard, D. C., & Blanchard, R. J. (1988). Ethoexperimental approaches to the biology of emotion. *Annual Review of Psychology*, *39*, 43–68.

Blanchard, D. C., & Blanchard, R. J. (1989). Experimental animal models of aggression: What do they say about human behaviour? In J. Archer & K. Browne (Eds.), *Human aggression: Naturalistic approaches* (pp. 94–121). London: Routledge.

Blanchard, D. C., & Blanchard, R. J. (2003). What can animal aggression research tell us about human aggression? *Hormones and Behavior*, *44*, 171–177.

Blanchard, D. C., Hynd, A. L., Minke, K. A., Minemoto, T., & Blanchard, R. J. (2001). Human defensive behaviors to threat scenarios show parallels to fear- and anxiety-related defense patterns of non-human mammals. *Neuroscience and Biobehavioral Reviews*, *25*, 761–770.

Blanchard, D. C., & Takahashi, S. N. (1988). No change in intermale aggression after amygdala lesions which reduce freezing. *Physiology and Behavior*, *42*, 613–616.

Blair, C., Peters, R., & Granger, D. (2004). Physiological and neuropsychological correlates of approach/withdrawal tendencies in preschool: Further examination of the behavioral inhibition system/behavioral activation system scales for young children. *Developmental Psychobiology*, *45*, 113–124.

Blair, R. J., Morris, J. S., Frith, C. D., Perrett, D. I., & Dolan, R. J. (1999). Dissociable neural responses to facial expressions of sadness and anger. *Brain*, *122*, 883–893.

Blonder, L. X., Gur, R. E., & Gur, R. C. (1989). The effects of right and left hemiparkinsonism on prosody. *Brain and Language*, *36*, 193–207.

Breitenstein, C., Daum, I., & Ackermann, H. (1998). Emotional processing following cortical and subcortical brain damage: Contribution of the fronto-striatal circuitry. *Behavioural Neurology*, *11*, 29–42.

Buhmann, C., Glauche, V., Stürenburg, H. J., Oechsner, M., Weiller, C., & Büchel, C. (2003). Pharmacologically modulated fMRI—cortical responsiveness to levodopa in drug-naïve hemiparkinsonian patients. *Brain*, *126*, 451–461.

Calder, A. J., Young, A. W., Rowland, D., Perrett, D. I., Hodges, J. R., & Etcoff, N. L. (1996). Facial emotion recognition after bilateral amygdala damage: Differentially severe impairment of fear. *Cognitive Neuropsychology*, *13*, 699–745.

Calder, A. J., Keane, J., Cole, J., Campbell, R., & Young, A. W. (2000). Facial expression recognition by people with Möbius syndrome. *Cognitive Neuropsychology*, *17*, 73–87.

Calder, A. J., Keane, J., Manes, F., Antoun, N., & Young, A. W. (2000). Impaired recognition and experience of disgust following brain injury. *Nature Neuroscience*, *3*, 1077–1078.

Calder, A. J., Lawrence, A. D., & Young, A. W. (2001). Neuropsychology of fear and loathing. *Nature Reviews Neuroscience*, *2*, 352–363.

Calder, A. J., Keane, J., Lawrence, A. D., & Manes, F. (2004). Impaired recognition of anger following damage to the ventral striatum. *Brain*, *127*, 1958–1969.

Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *Journal of Personality and Social Psychology*, 67, 319–333.

Carver, C. S. (2004). Negative affects deriving from the behavioral approach system. *Emotion*, *4*, 3–22.

Chevalier-Skolnikoff, S. (1973). Facial expression of emotion in nonhuman primates. In P. Ekman (Ed.), *Darwin and facial expression: A century of research in review* (pp. 11–89). New York: Academic Press.

Cloninger, C. R. (1987a). A systematic method for clinical description and classification of personality variants. *Archives of General Psychiatry*, *44*, 573–588.

Cloninger, C. R. (1987b). *The tridimensional personality questionnaire, version IV*. St. Louis, MO: Washington University School of Medicine.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.

Daffner, K. R., Mesulam, M. M., Holcomb, P. J., Calvo, V., Acar, D., Chabrerie, A., et al. (2000). Disruption of attention to novel events after frontal lobe injury in humans. *Journal of Neurology, Neurosurgery, and Psychiatry*, *68*, 18–24.

Dahlen, E. R., Martin, R. C., Ragan, K., & Kuhlman, M. M. (2004). Boredom proneness in anger and aggression: Effects of impulsiveness and sensation seeking. *Personality and Individual Differences*, *37*, 1615–1627.

Darwin, C. (1872/1965). *The expression of the emotions in man and animals*. Chicago: Chicago University Press.

Davis, E. S., & Marler, C. A. (2004). C-fos changes following an aggressive encounter in female California mice: A synthesis of behavior, hormone changes and neural activity. *Neuroscience*, *127*, 611–624.

Davis, M. (2000). The role of the amygdala in conditioned and unconditioned fear and anxiety. In J. P. Aggleton (Ed.), *The amygdala: A functional analysis* (2nd ed., pp. 213–287). Oxford: Oxford University Press.

Dewick, H. C., Hanley, J. R., Davies, A. D. M., Playfer, J., & Turnbull, C. (1991). Perception and memory for faces in Parkinson's disease. *Neuropsychologia*, *29*, 785–802.

Dimberg, U., Thunberg, M., & Elmehed, K. (2000). Unconscious facial reactions to emotional facial expressions. *Psychological Science*, *11*, 86–89.

Dujardin, K., Blairy, S., Defebvre, L., Duhem, S., Noël, Y., Hess, U., et al. (2004). Deficits in decoding emotional facial expressions in Parkinson's disease. *Neuropsychologia*, *42*, 239–250.

Dujardin, K., Blairy, S., Defebvre, L., Krystkowiak, P., Hess, U., Blond, S., et al. (2004). Subthalamic nucleus stimulation induces deficits in decoding emotional facial expressions in Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychiatry*, *75*, 202–208.

Ekman, P. (1972). Universals and cultural differences in facial expressions of emotion. In J. Cole (Ed.), *Nebraska syomposium on motivation, 1971* (pp. 207–283). Lincoln, Neb.: University of Nebraska Press.

Ekman, P. (1997). Should we call it expression or communication? *Innovations in Social Science Research*, *10*, 333–344.

Ekman, P., & Friesen, W. (1976). *Pictures of facial affect*. Palo Alto, CA: Consulting Psychologists Press.

Ekman, P., Levenson, R. W., & Friesen, W. V. (1983). Autonomic nervous system activity distinguishes among emotions. *Science*, *221*, 1208–1210.

Fahn, S., Elton, R. L., & Members of the UPDRS Development Committee. (1987). Unified Parkinson's Disease Rating Scale. In S. Fahn, C. D. Marsden, D. B. Calne, & M. Goldstein (Eds.), *Recent developments in Parkinson's disease* (pp. 153–164). Florham Park, New York: Macmillan Healthcare Information.

Felip, C. M., Rodríguez-Arias, M., Aguilar, M. A., & Miñarro, J. (2001). Anti-aggressive and motor effects of the DA release inhibitor CGS 10746B. *Aggressive Behavior*, *27*, 382–390.

Ferrari, P. F., van Erp, A. M., Tornatzky, W., & Miczek, K. A. (2003). Accumbal dopamine and serotonin in anticipation of the next aggressive episode in rats. *European Journal of Neuroscience*, *17*, 371–378.

Fish, E. W., DeBold, J. F., & Miczek, K. A. (2002). Aggressive behavior as a reinforcer in mice: Activation by allopregnanolone. *Psychopharmacology*, *163*, 459–466.

Frank, M. G., & Stennett, J. (2001). The forced-choice paradigm and the perception of facial expressions of emotion. *Journal of Personality and Social Psychology*, *80*, 75–85.

Frank, M. J., Seeberger, L. C., & O'Reilly, R. C. (2004). By carrott or by stick: Cognitive reinforcement learning in Parkinsonism. *Science*, *306*, 1940–1943.

Fuji, C., Harada, S., Ohkoshi, N., Hayashi, A., & Yoshizawa, K. (2000). Cross-cultural traits for personality of patients with Parkinson's disease in Japan. *American Journal of Medical Genetics (Neuropsychiatric Genetics)*, *96*, 1–3.

Gancher, S. T., Nutt, J. G., & Woodward, W. R. (1987). Peripheral pharmacokinetics of levodopa in untreated, stable, and fluctuating parkinsonian patients. *Neurology*, *37*, 940–944.

Giancola, P. R., Zeichner, A., Newbolt, W. H., & Stennett, R. B. (1994). Construct validity of the dimensions of Cloninger's tridimensional personality questionnaire. *Personality and Individual Differences*, *17*, 627–636.

Goerendt, I. K., Lawrence, A. D., & Brooks, D. J. (2004). Reward processing in health and Parkinson's disease: Neural organization and reorganization. *Cerebral Cortex*, *14*, 73–80.

Goldman, A. I., & Sripada, C. S. (2005). Simulationist models of face-based emotion recognition. *Cognition*, *94*, 193–213.

Goodwin, F. K., Murphy, D. L., Brodie, K. H., & Bunney, W. E., Jr. (1970). L-dopa, catecholamines, and behavior: A clinical and biochemical study in depressed patients. *Biological Psychiatry*, *2*, 341–366.

Gordon, R. M. (1987). *The structure of emotions*. Cambridge: Cambridge University Press.

Gordon, R. M. (1992). The simulation theory: Objections and misconceptions. *Mind and Language*, *7*, 11–34.

Griffiths, P. E. (2001). From adaptive heuristic to phylogenetic perspective: Some lessons from the evolutionary psychology of emotion. In H. R. Holcomb III (Ed.), *Conceptual challenges in evolutionary psychology* (pp. 309–325). Dordrecht: Kluwer.

Harmer, C. J., Thilo, K. V., Rothwell, J. C., & Goodwin, G. M. (2001). Transcranial magnetic stimulation of medial-frontal cortex impairs the processing of angry facial expressions. *Nature Neuroscience*, *4*, 17–18.

Harmon-Jones, E. (2003). Anger and the behavioral approach system. *Personality and Individual Differences*, *35*, 995–1005.

Harmon-Jones, E., Sigelman, J. D., Bohlig, A., & Harmon-Jones, C. (2003). Anger, coping, and frontal cortical activity: The effect of coping potential on anger-induced left frontal activity. *Cognition and Emotion*, *17*, 1–24.

Henenlotter, A., Schroeder, U., Erhard, P., Haslinger, B., Stahl, R., Weindl, A., et al. (2004). Neural correlates associated with impaired disgust processing in pre-symptomatic Huntington's disease. *Brain*, *127*, 1446–1453.

Heweg, J., Hagemann, D., Seifert, J., Naumann, E., & Bartussek, D. (2004). On the selective relation of frontal cortical asymmetry and anger-out versus anger-control. *Journal of Personality and Social Psychology*, *87*, 926–939.

Hornykiewicz, O., & Kish, S. J. (1986). Biochemical pathophysiology of Parkinson's disease. *Advances in Neurology*, *45*, 19–34.

Hughes, A. J., Daniel, S. E., Kilford, L., & Lees, A. J. (1992). Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery, and Psychiatry*, *55*, 181–184.

Ikemoto, S., & Panksepp, J. (1999). The role of nucleus accumbens dopamine in motivated behavior: A unifying interpretation with special reference to reward-seeking. *Brain Research Reviews*, *31*, 6–41.

Jacobs, D. H., Shuren, J., Bowers, D., & Heilman, K. M. (1995). Emotional facial imagery, perception, and expression in Parkinson's disease. *Neurology*, *45*, 1696–1702.

Joireman, J., Anderson, J., & Strathman, A. (2003). The aggression paradox: Understanding links among aggression, sensation seeking, and the consideration of future consequences. *Journal of Personality and Social Psychology*, *84*, 1287–1302.

Kan, Y., Kawamura, M., Hasegawa, Y., Mochizuki, S., & Nakamura, K. (2002). Recognition of emotion from facial, prosodic and written verbal stimuli in Parkinson's disease. *Cortex*, *38*, 623–630.

Kazlauckas, V., Schuh, J., Dall'Igna, O. P., Pereira, G. S., Bonan, C. D., & Lara, D. R. (2005). Behavioral and cognitive profile of mice with high and low exploratory phenotypes. *Behavioural Brain Research*, *162*, 272–278.

Kelly, R. M., & Strick, P. L. (2004). Macro-architecture of basal ganglia loops with the cerebral cortex: Use of rabies virus to reveal multisynaptic circuits. *Progress in Brain Research*, *143*, 449–459.

Kikuchi, A., Takeda, A., Kimpara, T., Nakagawa, M., Kawashima, R., Sugiura, M., et al. (2001). Hypoperfusion in the supplementary motor area, dorsolateral prefrontal cortex and insular cortex in Parkinson's disease. *Journal of the Neurological Sciences*, *193*, 29–36.

Krolak-Salmon, P., Henaff, M. A., Isnard, J., Tallon-Baudry, C., Guenot, M., Vighetto, A., et al. (2003). An attention modulated response to disgust in human ventral anterior insula. *Annals of Neurology*, *53*, 446–453.

Kudryavtseva, N. N. (2000). An experimental approach to the study of learned aggression. *Aggressive Behavior*, *26*, 241–256.

Kudryavtseva, N. N., Lipina, T. V., & Koryakina, L. A. (1999). Effects of haloperidol on communicative and aggressive behavior in male mice with different experiences of aggression. *Pharmacology, Biochemistry and Behavior*, *63*, 229–236.

Lawrence, A. D., & Calder, A. J. (2004). Homologizing human emotions. In D. Evans & P. Cruse (Eds.), *Emotion, evolution and rationality* (pp. 15–47). Oxford: Oxford University Press.

Lawrence, A. D., Calder, A. J., McGowan, S. W., & Grasby, P. M. (2002). Selective disruption of the recognition of facial expressions of anger. *NeuroReport*, *13*, 881–884.

Lawrence, A. D., Evans, A. H., & Lees, A. J. (2003). Compulsive use of dopamine replacement therapy in Parkinson's disease: Reward systems gone awry? *Lancet Neurology*, *2*, 595–604.

Leentjens, A. F. G., Verhey, F. R. J., Luijckx, J.-G., & Troost, J. (2000). The validity of the Beck Depression Inventory as a screening and diagnostic instrument for depression in patients with Parkinson's disease. *Movement Disorders*, *15*, 1221–1224.

Lewis, D. A., & Sesack, S. R. (1997). Dopamine systems in the primate brain. In F. E. Bloom, A. Björklund, & T. Hökfelft (Eds.), *Handbook of chemical neuroanatomy, Vol. 13: The primate nervous system, part I* (pp. 263–375). Amsterdam: Elsevier.

Leyton, M., Boileau, I., Benkelfat, C., Diksic, M., Baker, G., & Dagher, A. (2002). Amphetamine-induced increases in extracellular dopamine, drug wanting, and novelty seeking: A PET/[^{11}C]raclopride study in healthy men. *Neuropsychopharmacology*, *27*, 1027–1035.

Louilot, A., LeMoal, M., & Simon, H. (1986). Differential reactivity of dopaminergic neurons in the nucleus accumbens in response to different behavioral situations. An in vivo voltammetric study in freely moving rats. *Brain Research*, *397*, 395–400.

Madeley, P., Ellis, A. W., & Mindham, R. H. S. (1995). Facial expressions and Parkinson's disease. *Behavioural Neurology*, *8*, 115–119.

Martínez, M., Guillén-Salazar, F., Salvador, A., & Simón, V.M. (1995). Successful intermale aggression and conditioned place preference in mice. *Physiology & Behavior*, 58, 323–328.

Masur, J., Maroni, J. B., & Benedito, M. A. C. (1975). Genetically selected winner and loser rats in the tunnel competition: Influence of apomorphine and dopa. *Behavioral Biology*, *14*, 21–30.

Meunier, M., & Bachevalier, J. (2002). Comparison of emotional responses in monkeys with rhinal cortex or amygdala lesions. *Emotion*, *2*, 147–161.

Miczek, K. A., Fish, E. W., De Bold, J. F., & De Almeida, R. M. (2002). Social and neural determinants of aggressive behavior: Pharmacotherapeutic targets at serotonin, dopamine and gamma-aminobutyric acid systems. *Psychopharmacology*, *163*, 435–458.

Mitchell, I. J., Heims, H., Neville, E. A., & Rickards, H. (2005). Huntington's disease patients show impaired perception of disgust in the gustatory and olfactory modalities. *Journal of Neuropsychiatry and Clinical Neurosciences*, *17*, 119–121.

Morris, J. S., Öhman, A., & Dolan, R. J. (1998). Conscious and unconscious emotional learning in the human amygdala. *Nature*, *393*, 467–470.

Murphy, C. A., Russig, H., Pezze, M.-A., Ferger, B., & Feldon, J. (2003). Amphetamine withdrawal modulates FosB expression in mesolimbic dopaminergic target nuclei: Effects of different schedules of administration. *Neuropharmacology*, *44*, 926–939.

Murphy, F. C., Nimmo-Smith, I., & Lawrence, A. D. (2003). Functional neuroanatomy of emotions: A meta-analysis. *Cognitive, Affective, and Behavioral Neuroscience*, *3*, 207–233.

Mutschler, N. H., & Miczek, K. A. (1998). Withdrawal from IV cocaine "binges" in rats: Ultrasonic distress calls and startle. *Psychopharmacology*, *135*, 161–168.

Nelson, H. (1991). *National adult reading test (NART), 2nd ed., test manual*. Windsor: NFER-Nelson.

Oakes, M. E., & Coover, G. D. (1997). Effects of small amygdala lesions on fear, but not aggression, in the rat. *Physiology and Behavior*, *61*, 45–55.

Öhman, A. (1986). Face the beast and fear the face: Animal and social fears as prototypes for evolutionary analyses of emotion. *Psychophysiology*, *23*, 123–145.

Otter, C., Huber, J., & Bonner, A. (1995). Cloninger's tridimensional personality questionnaire: Reliability in an English sample. *Personality and Individual Differences*, *18*, 471–480.

Pell, M. D., & Leonard, C. L. (2005). Facial expression decoding in early Parkinson's disease. *Cognitive Brain Research*, *23*, 327–340.

Phillips, M. L., Williams, L., Senior, C., Bullmore, E. T., Brammer, M. J., Andrew, C., et al. (1999). A differential neural response to threatening and non-threatening negative facial expressions in paranoid and non-paranoid schizophrenics. *Psychiatry Research: Neuroimaging*, *92*, 11–31.

Pine, D. S., Mogg, K., Bradley, B. P., Montgomery, L., Monk, C. S., McClure, E., et al. (2005). Attention bias to threat in maltreated children: Implications for vulnerability to stress-related psychopathology. *American Journal of Psychiatry*, *162*, 291–296.

Price, K. S., Farley, I. J., & Hornykiewicz, O. (1978). Neurochemistry of Parkinson's disease: Relation between striatal and limbic dopamine. *Advances in Biochemical Psychopharmacology*, *19*, 293–300.

Putnam, P., Hermans, E., & van Honk, J. (2004). Emotional Stroop performance for masked angry faces: It's BAS, not BIS. *Emotion*, *4*, 305–311.

Redolat, R., Brain, P. F., & Simón, V. M. (1991). Sulpiride has an antiaggressive effect in mice without markedly depressing motor activity. *Neuropsychopharmacology*, *30*, 41–46.

Remy, P., Doder, M., Lees, A., Turjanski, N., & Brooks, D. (2005). Depression in Parkinson's disease: Loss of dopamine and noradrenaline innervation in the limbic system. *Brain*, *128*, 1314–1322.

Rosenthal, R., Rosnow, R. L., & Rubin, D. B. (2000). *Contrasts and effect sizes in behavioral research*. Cambridge: Cambridge University Press.

Rüb, U., Del Tredici, K., Schultz, C., Ghebremedhin, E., de Vos, R. A. I., Jansen Steur, E., et al. (2002). Parkinson's disease: The thalamic components of the limbic loop are severely impaired by α-synuclein immunopositive inclusion body pathology. *Neurobiology of Aging*, *23*, 245–254.

Saku, M., & Ellgring, H. (1992). Emotional reactions to odours in Parkinson's disease: A clinical application of ethological methods. *Journal of Ethology*, *10*, 47–52.

Scatton, B., Javoy-Agid, F., Rouquier, L., Dubois, B., & Agid, Y. (1983). Reduction of cortical dopamine, noradrenaline, serotonin and their metabolites in Parkinson's disease. *Brain Research*, *275*, 321–328.

Scott, S., Caird, F. I., & William, S. B. (1984). Evidence for an apparent sensory speech disorder in Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, *47*, 840–843.

Schaefer, A., Collette, F., Philippot, P., Van der Linden, M., Laureys, S., Delfiore, G., et al. (2003). Neural correlates of "hot" and "cold" emotional processing: A multilevel approach to the functional anatomy of emotion. *NeuroImage*, *18*, 938–949.

Shipley, B. (2000). *Cause and correlation in biology: A user's guide to path analysis, structural equations and causal inference*. Cambridge: Cambridge University Press.

Sienkiewicz-Jarosz, H., Scinska, A., Kuran, W., Ryglewicz, D., Rogowski, A., Wrobel, E., et al. (2005). Taste responses in patients with Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, *76*, 40–46.

Simón, V., Minarro, J., Redolat, R., & Garmendia, L. (1989). An ethopharmacological study of the effects of three neuroleptics (haloperidol, clozapine and sulpiride) on aggressive encounters in male mice. In R. J. Blanchard, P. F. Brain, D. C. Blanchard, & S. Parmigiani (Eds.), *Ethoexperimental approaches to the study of behavior* (pp. 474–483). Dordrecht: Kluwer.

Smits, D. J. M., & Kuppens, P. (2005). The relations between anger, coping with anger, and aggression, and the BIS/BAS system. *Personality and Individual Differences*, *39*, 783–793.

Sprengelmeyer, R., Young, A. W., Calder, A. J., Karnat, A., Lange, H., Homberg, V., et al. (1996). Loss of disgust: Perception of faces and emotions in Huntington's disease. *Brain*, *119*, 1647–1665.

Sprengelmeyer, R., Young, A.W., Schroeder, U., Grossenbacher, P.G., Federlein, J., Büttner T., & Przuntek, H. (1999). Knowing no fear. *Proceedings of the Royal Society B: Biological Sciences*, 266, 2451–2456.

Sprengelmeyer, R., Young, A. W., Mahn, K., Schroeder, U., Woitalla, D., Büttner, T., et al. (2003). Facial expression recognition in people with medicated and unmedicated Parkinson's disease. *Neuropsychologia*, *41*, 1047–1057.

St. Clair, J., Borod, J. C., Sliwinski, M., Cote, L. J., & Stern, Y. (1998). Cognitive and affective functioning in Parkinson's disease patients with lateralized motor signs. *Journal of Clinical and Experimental Neuropsychology*, *20*, 320–327.

Stein, M. B., Goldin, P. R., Sareen, J., Zorrilla, L. T., & Brown, G. G. (2002). Increased amygdala activation to angry and contemptuous faces in generalized social phobia. *Archives of General Psychiatry*, *59*, 1027–1034.

Svrakic, D. M., Przybeck, T. R., Whitehead, C., & Cloninger, C. R. (1999). Emotional traits and personality dimensions. In C. R. Cloninger (Ed.), *Personality and psychopathology* (pp. 245–265). Washington, DC: American Psychiatric Press.

Thieben, M. J., Duggins, A. J., Good, C. D., Gomes, L., Mahant, N., Richards, F., et al. (2002). The distribution of structural neuropathology in pre-clinical Huntington's disease. *Brain*, *125*, 1815–1828.

Todes, C. J., & Lees, A. J. (1985). The pre-morbid personality of patients with Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, *48*, 97–100.

Travers, J. B., Akey, L. R., Chen, S. C., Rosen, S., Paulson, G., & Travers, S. P. (1993). Taste preferences in Parkinson's disease patients. *Chemical Senses*, *18*, 47–55.

Tsang, W. K., & Stutz, R. M. (1984). Subject control as a determinant of the reinforcing properties of intracranial stimulation. *Physiology and Behavior*, *32*, 795–802.

van Erp, A. M., & Miczek, K. A. (2000). Aggressive behavior, increased accumbal dopamine, and decreased cortical serotonin in rats. *Journal of Neuroscience*, *20*, 9320–9325.

von Collani, G., & Werner, R. (2005). Self-related and motivational constructs as determinants of aggression. An analysis and validation of a German version of the Buss-Perry aggression questionnaire. *Personality and Individual Differences*, *38*, 1631–1643.

Whalen, P. J., Shin, L. M., McInerney, S. C., Fischer, H., Wright, C. I., & Rauch, S. L. (2001). A functional MRI study of human amygdala responses to facial expressions of fear versus anger. *Emotion*, *1*, 70–83.

Wills, T. A., Vaccaro, D., & McNamara, G. (1994). Novelty seeking, risk taking, and related constructs as predictors of adolescent substance use: An application of Cloninger's theory. *Journal of Substance Abuse*, *6*, 1–20.

Williams, L. M., Das, P., Liddell, B., Olivieri, G., Peduto, A., Brammer, M. J., et al. (2005). BOLD, sweat and fears: fMRI and skin conductance distinguish facial fear signals. *NeuroReport*, *16*, 49–52.

Wilson, G. D., Barrett, P. T., & Gray, J. A. (1989). Human reactions to reward and punishment: A questionnaire examination of Gray's personality theory. *British Journal of Psychology*, *80*, 509–515.

Wingrove, J., & Bond, A. J. (1998). Angry reactions to failure on a cooperative computer game: The effect of trait hostility, behavioural inhibition, and behavioural activation. *Aggressive Behavior*, *24*, 27–36.

Yip, J. T. H., Lee, T. M. C., Ho, S.-L., Tsang, K.-L., & Li, L. S. W. (2003). Emotion recognition in patients with idiopathic Parkinson's disease. *Movement Disorders*, *18*, 1115–1122.

Zuckerman, M. (1999). Incentive motivation: just extraversion? *Behavioral and Brain Sciences*, 22: 539–540.